REMARKS

By the amendments presented, Claim 27 has been canceled without prejudice, and the pharmaceutical active limitations of this canceled claim have been incorporated into Claim 21.

Attached hereto is a mark d-up version of the hanges made to the claims as a result of the current amendments. The attached page is captioned **"Version with Markings to Show Claim Changes Made"**.

Upon entry of the amendments presented, Claims 21-26 and 28-36 remain in the present application. No additional claims fee is due.

Invention Synopsis

The present invention is directed to stable liquid compositions which comprise a pharmaceutical active and a reducing agent, wherein the reducing agent provides for improved stability of these compositions especially when the compositions are formulated into various product forms such as liquid elixirs for treating symptoms associated with respiratory illnesses.

It has been found that a reducing agent can be included in liquid compositions containing a pharmaceutical active to enhance long term stability of the composition, provided that the reducing agent is solubilized in a solvent system separately from a solvent system used to solubilize the active. The solubilzation of the reducing agent in one solvent phase, and the active in another solvent phase, results in a stable, homogenous, liquid composition that is highly effective in the delivery of pharmaceutical active ingredients, especially pharmaceutical active ingredients such as antitussives, antihistamines, non-sedating antihistamines, decongestants, expectorants, analgesic mucolytics, antipyretics, anti-inflammatory agents, and local anesthetics.

Formal Matters

Rejection under 35 U.S.C. 112 (1st paragraph)

Claims 8 and 21-36 have been rejected under 35 U.S.C. 112 (1st paragraph) for an alleged failure to provide a description in the specification of the solvents defined in these claims, except for the exemplified disclosure at page 12, line 1 describing water as a solvent. Applicants submit that Claim 8 has been canceled without prejudice in the Response dated June 19, 2001, thus obviating this rejection as it would apply to this canceled claim. Applicants respectfully traverse this rejection as it would apply to pending Claims 21-36, and state that at page 7, lines 21-35, and page 8, lines 1-2, solvents as claimed in Claims 21-36 are fully described in a manner for enablement by the skilled artisan to incorporate such clearly described solvent into an oral composition as claimed by Applicants, as well as in a manner for art rejection by the Examiner citing prior art disclosing Applicants' defined solvent agents. Applicants further submit that at page 6, lines 11-21, the specification provides sufficient description of the concentration of the claimed pharmaceutical active component in the disc l sed solvent system. Applicants further submit, contrary to the Examiner's contention, that Examples I-XIII clearly exemplify oral compositions containing solvents

moot cl. 8 canceled

moot cls 21-36

as described in the specification, wherein the solvents include compounds such as ethanol and propylene glycol with and without the addition of water. Based on these complete descriptions of the solvents defined in Claims 21-36, Applicants submit that the specification provides full enablement for an oral composition comprising Applicants' claimed solvent. Accordingly, this 35 U.S.C. 112 (1st paragraph) rejection should be withdrawn.

Rejections under 35 U.S.C. 112 (2nd paragraph)

Claims 8 and 21-36 have been rejected under 35 U.S.C. 112 (2nd paragraph) as being indefinite for recitation of the "phase" terminology defined in these claims. Responsive to this rejection, Applicants have amended Claim 21 and dependent claims therefrom to delete reference to "the reducing agent being solubilized in a phase of the composition other than the phase of the composition in which the pharmaceutical active is solubilized", thus obviating this rejection as it would apply to amended Claims 21-36. Applicants submit that Claim 8 has been canceled without prejudice in the Response dated June 19, 2001, thus obviating this rejection as it would apply to this canceled claim.

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Claim 8 has also been rejected under 35 U.S.C. 112 (2nd paragraph) as being indefinite for its alleged dependency upon a canceled claim. As previously stated, Claim 8 has been canceled without prejudice in the Response dated June 19, 2001, thus obviating this rejection as it would apply to this canceled claim.

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Art Rejection

Claims 21-36 have been rejected under 35 U.S.C. 102 as being anticipated by Gallo-Torres et al. (U.S. Patent 4,310,543). The Examiner contends that Gallo-Torres et al. disclose an oral composition as claimed by Applicants, wherein the composition comprises a pharmaceutical active, an active solvent such as polyethylene glycol, and a reducing agent such as bisulfite, thiourea or tert-butyl hydroquinone. Applicants respectfully traverse this rejection as it would apply to remaining amended Claims 21-26 and 28-36. Applicants submit that Claim 27 has been canceled without prejudice, thus obviating this rejection as it would apply to this claim.

Gallo-Torres et al. disclose pharmaceutical compositions which are orally administered, and which comprise a prostaglandin pharmaceutical active and an ascorbic acid or ascorbyl palmitate stabilizer dissolved in a solvent such as polyethylene glycol. Gallo-Torres et al. further disclose that up to about 0.5% by weight of other stabilizes can be included in the oral pharmaceutical compositions wherein the other stabilizers include various compounds such as bisulfite, hydroquinone, 2 tert-butyl hydroquinone, and thiourea. A typical manner of making an oral pharmaceutical composition of Gallo-Torres et al. include adding an ascorbate and another stablilizer to liquid polyethylene glycol, and thereafter adding the prostaglandin active ingredient. Gallo-Torres et al., however, fail to disclose an oral composition comprising a pharmaceutical active selected from the group consisting of antitussives, antihistamines, non-sedating antihistamines, decongestants,

expectorants, analgesic mucolytics, antipyretics, anti-inflammatory agents, local anesthetics, and mixtures thereof.

Applicants submit that the Gallo-Torres et al. referenc fails to anticipate Applicants' remaining amended Claims 21-26 and 28-36, wherein these claims are directed to oral compositions which comprise a *select* pharmaceutical active; a hydrophilic, water-miscible, anhydrous active solvent; and a reducing agent. Gallo-Torres et al. teach oral pharmaceutical compositions comprising a generally anti-secretory prostaglandin pharmaceutical active, wherein the prostaglandin and a stabilizer are dissolved in a solvent such as polyethylene glycol. By contrast, Applicants' amended Claims 21-26 and 28-36 are now directed to oral compositions comprising *select* pharmaceutical actives excluding a prostaglandin pharmaceutical active agent.

Moreover, to anticipate Applicants' remaining amended Claims 21-26 and 28-36, the Gallo-Torres et al. reference should teach each and every limitation recited in these claims. Gallo-Torres et al. fail to teach Applicants' now claimed limitation of a pharmaceutical active selected from the group consisting of antitussives, antihistamines, non-sedating antihistamines, decongestants, expectorants, analgesic mucolytics, antipyretics, anti-inflammatory agents, local anesthetics, and mixtures thereof.

In view of the foregoing remarks, Applicants submit that the Gallo-Torres et al. reference fails to teach each and every limitation of Applicants' remaining amended Claims 21-26 and 28-36. The rejection of these claims as being anticipated by Gallo-Torres et al. is improper and should, therefore, be withdrawn.

Conclusions

Applicants have made an earnest effort to place the application in proper form and to distinguish the claimed invention from the applied prior art. WHEREFORE, reconsideration of this application, withdrawal of the rejections under 35 U.S.C. 112 (1st and 2nd paragraphs) and 35 U.S.C. 102, and allowance of Claims 21-26 and 28-36 are respectfully requested.

Respectfully submitted,
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Version with Markings to Sh w Claim Changes Made

Claim 27 has been canceled without prejudice.

Claim 21 has been amended as follows:

Claim 21. (2nd Amendment) An oral composition comprising:

(a) a pharmaceutical active selected from the group consisting of antitussives, antihistamines, non-sedating antihistamines, decongestants, expectorants, analgesic mucolytics, antipyretics, anti-inflammatory agents, local anesthetics, and mixtures thereof;

(b) [in] a hydrophilic, water-miscible, anhydrous solvent wherein the pharmaceutical active in its un-ionized form has a percent solubility value in the solvent at ambient temperature that is equal to or greater than 0.075% and the pharmaceutical active is in its free, un-ionized form as a monomolecular dispersion in the solvent[,]; and

(c) a reducing agent wherein the reducing agent has an E^0 value equal to or greater than about -0.119V [and is solubilized in a phase of the composition other than the phase of the composition in which the pharmaceutical active is solubilized].